

which had the following nucleotide sequence:

hybridization probe

5'-TGGACACCTTCAGTATTGATGCCAAGACAGGCCAGGTCATTCTGCGTCGA-3' (SEQ ID NO:428).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO731 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human bone marrow tissue (LIB255). The cDNA libraries used to isolate the cDNA clones were constructed by standard methods using commercially available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a NotI site, linked with blunt to SalI hemikinased adaptors, cleaved with NotI, sized appropriately by gel electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD; pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., *Science*, 253:1278-1280 (1991)) in the unique XhoI and NotI sites.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO731 [herein designated as UNQ395 (DNA48331-1329)] (SEQ ID NO:424) and the derived protein sequence for PRO731.

The entire nucleotide sequence of UNQ395 (DNA48331-1329) is shown in Figure 170 (SEQ ID NO:424). Clone UNQ395 (DNA48331-1329) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 329-331 and ending at the stop codon at nucleotide positions 3881-3883 (Figure 170). The predicted polypeptide precursor is 1184 amino acids long (Figure 171). The full-length PRO731 protein shown in Figure 171 has an estimated molecular weight of about 129,022 daltons and a pI of about 5.2. Clone UNQ395 (DNA48331-1329) was deposited with the ATCC on March 31, 1998. Regarding the sequence, it is understood that the deposited clone contains the correct sequence, and the sequences provided herein are based on known sequencing techniques.

Analysis of the amino acid sequence of the full-length PRO731 polypeptide suggests that portions of it possess significant identity and similarity to members of the protocadherin family, thereby indicating that PRO731 may be a novel protocadherin.

Still analyzing the amino acid sequence of SEQ ID NO:425, the putative signal peptide is at about amino acids 1-13 of SEQ ID NO:425. The transmembrane domain is at amino acids 719-739 of SEQ ID NO:425. The N-glycosylation of SEQ ID NO:425 are as follows: 415-418, 582-586, 659-662, 662-665, and 857-860. The cadherin extracellular repeated domain signatures are at about amino acids (of SEQ ID NO:425): 123-133, 232-242, 340-350, 448-458, and 553-563. The corresponding nucleotides can be routinely determined given the sequences provided herein.

EXAMPLE 69: Isolation of cDNA Clones Encoding Human PRO218

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA17411. Two proprietary Genentech EST sequences were employed in the consensus assembly and are shown in Figure 174 and 175. Based on the DNA17411 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that

contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO218.

A pair of PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-AAGTGGAGCCGGAGCCTTCC-3' (SEQ ID NO:433);

reverse PCR primer 5'-TCGTTGTTTATGCAGTAGTCGG-3' (SEQ ID NO:434).

- 5 Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA17411 sequence which had the following nucleotide sequence:

hybridization probe

5'-ATTGTTTAAAGACTATGAGATACGTCAGTATGTTGTACAGG-3' (SEQ ID NO:435).

- 10 In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO218 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue (LIB28).

- 15 DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO218 [herein designated as UNQ192 (DNA30867-1335)] (SEQ ID NO:429) and the derived protein sequence for PRO218.

- 20 The entire nucleotide sequence of UNQ192 (DNA30867-1335) is shown in Figure 172 (SEQ ID NO:429). Clone UNQ192 (DNA30867-1335) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 150-152 and ending at the stop codon at nucleotide positions 1515-1517 (Figure 172). The predicted polypeptide precursor is 455 amino acids long (Figure 173). The full-length PRO218 protein shown in Figure 173 has an estimated molecular weight of about 52,917 daltons and a pI of about 9.5. Clone UNQ192 (DNA30867-1335) has been deposited with the ATCC on April 28, 1998. Regarding the sequence, it is understood that the deposited clone contains the correct sequence, and the sequences provided herein are based on known sequencing techniques.

- 25 Analysis of the amino acid sequence of the full-length PRO218 polypeptide suggests that PRO218 may be a novel transmembrane protein.

- 30 Still analyzing the amino acid sequence of SEQ ID NO:430, the putative signal peptide is at about amino acids 1 through 23 of SEQ ID NO:430. Transmembrane domains are potentially at about amino acids 37-55, 81-102, 150-168, 288-311, 338-356, 375-398, and 425-444 of SEQ ID NO:430. N-glycosylation sites are at about amino acids 67, 180, and 243 of SEQ ID NO:430. Eukaryotic cobalamin-binding protein is at about amino acids 151-160 of SEQ ID NO:430. The corresponding nucleotides can be routinely determined given the sequences provided herein.

EXAMPLE 70: Isolation of cDNA Clones Encoding Human PRO768

- 35 A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA43448. Based on the DNA43448 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO768.

A pair of PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-GGCTGACACCGCAGTGCTCTTCAG-3' (SEQ ID NO:438);

reverse PCR primer 5'-GCTGCTGGGGACTGCAATGTAGCTG-3' (SEQ ID NO:439).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA43448 consensus sequence which had the following nucleotide sequence:

5 hybridization probe

5'-CATCCTCCATGTCTCCCATGAGGTCTCTATTGCTCCACGAAGCATC-3' (SEQ ID NO:440).

10 In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO768 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human bone marrow tissue (LIB255).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO768 [herein designated as UNQ406 (DNA55737-1345)] (SEQ ID NO:436) and the derived protein sequence for PRO768.

15 The entire nucleotide sequence of UNQ406 (DNA55737-1345) is shown in Figure 176 (SEQ ID NO:436). Clone UNQ406 (DNA55737-1345) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 20-22 and ending at the stop codon at nucleotide positions 3443-3445 (Figure 176). The predicted polypeptide precursor is 1141 amino acids long (Figure 177). The full-length PRO768 protein shown in Figure 177 has an estimated molecular weight of about 124,671 daltons and a pI of about 5.82. Clone UNQ406 (DNA55737-1345) has been deposited with the ATCC on April 6, 1998. Regarding the sequence, it is understood that the deposited clone contains the correct sequence, and the sequences provided herein are based on known sequencing techniques.

20 Analysis of the amino acid sequence of the full-length PRO768 polypeptide suggests that portions of it possess significant sequence identity and similarity with integrin 7.

25 Still analyzing the amino acid sequence of SEQ ID NO:437, the putative signal peptide is at about amino acids 1-33 of SEQ ID NO:437. The transmembrane domain is at amino acids 1039-1064 of SEQ ID NO:437. N-glycosylation sites are at amino acids: 86-89, 746-749, 949-952, 985-988 and 1005-1008 of SEQ ID NO:437. Integrin alpha chain protein domains are identified at about amino acids: 1064-1071, 384-409, 1041-1071, 317-346, 443-465, 385-407, 215-224, 634-647, 85-99, 322-346, 470-479, 442-466, 379-408 and 1031-1047 of SEQ ID NO:437. The corresponding nucleotides can be routinely determined given the sequences provided herein.

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EXAMPLE 71: Isolation of cDNA Clones Encoding Human PRO771

35 A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA43330. Based on the DNA43330 sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO771.

A pair of PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-CAGCAATATTCAGAAGCGGCAAGGG-3' (SEQ ID NO:443);